REMARKS

The only issue outstanding in the Office Action mailed July 27, 2004, is the rejections of all claims under 35 U.S.C §103. The prior rejections under 35 U.S.C §112 have apparently been withdrawn.

Reconsideration of the rejections under 35 U.S.C §103 over each of Dennertein (British Medical Journal) and Gullberg, as well as over the Harvard Review of Psychiatry, is respectfully requested. At the outset, before discussion the merits of these rejections, Applicants wish to clear up an apparent misconception in the present Office Action. At page 3 of the Office Action, reasons why the prior declaration under 37 C.F.R. §1.132 was found not to be probative are listed. It is evident from this discussion of reasons that the Examiner has misapprehended the reason why the declaration was submitted. The Office Action criticizes the declaration because "no other gestagen is compared", and because the results "are not compared with any closest prior art, such as progesterone alone and in combination with estrogen." However, the prior declaration, it should be noted, is not discussed in the section of Applicants' prior response that deals with the art rejections. Instead, careful attention to Applicants' response filed April 22, 2004, shows that the declaration was submitted to provide evidence of *efficacy* of the present invention. See page 8 of the prior reply. This, the declaration does by showing that the combination of DRSP and estrogen is effective in treating PMDD. While this may not be considered to be "unexpected results", as argued at page 3 of the Office Action, of course, such results are irrelevant for a demonstration of efficacy.

In any event, as will be recalled, all cited references deal with various gestagens and/or estrogens for use in treating PMS. Contrary to the allegation on page 4 of the Office Action, the references do not teach a method which "embraces instantly claimed invention." It is evident from the Office Action, for example at page 4, that the Examiner believes the PMDD is a "severe form of PMS." This is untrue. As has been discussed at length, yet not commented upon in the present Office Action, it is well understood and recognized by researchers and practitioners in the field of Obstetrics and Gynecology that PMS and PMDD, while sharing some of the same signs

and symptoms, are not the same disease. Indeed, differences between the two indications are differences of kind, not mere degree. For example, PMDD usually comprises extremely distressing emotional behavioral symptoms including irritability, dysphoria, tension and mood liability which may be accompanied by physical complaints. Symptoms appear three to ten days ***PRIOR*** to the onset of menstrual bleeding and remit ***AFTER*** menses. Approximately, 3 to 8% of women of reproductive age are affected with PMDD (Steiner et al., *Inter. Clin. Psychopharm.* 15 (Suppl. 3):S15 - S17 (2000)). PMDD has a distinct clinical picture wherein timing of onset and cessation are ***UNIQUE***.

By contrast, PMS is a far more prevalent indication which affects approximately 75% of women of reproductive age. By contrast to PMDD, the symptoms appear ***LUTEAL*** phase ***CEASE*** with menses. This difference in onset and remission alone are submitted to constitute such considerable differences so as to prohibit any inference of motivation to employ a treatment for indication in the other. PMS possesses further clinical differences from PMDD, as set forth in page 3 of the declaration filed November 2, 2002.

The Office Action appears to misconstrue the relevance of overlap between some symptoms of PMS and PMDD. Overlap of symptoms is irrelevant for indications (i.e., diseases) which have different etiology. To take the PTO analysis to the extreme, a headache can be a symptom of either sinus blockage, or an incipient aneurysm. However, because aspirin is typically effective against sinus headache, this does not mean that it would be obvious to one of ordinary skill in the art to administer aspirin to a patient diagnosed to be at risk for an aneurysm. It is a mistake, as done in the Office Action to confuse the symptoms with the clinical indication (i.e., disease). PMDD, as explained above, has different onset and different symptoms, some of which may overlap, some of which do not, with PMS. Patients clinically diagnosed as suffering from PMDD are recognized in the art by the FDA as a different group than those suffering from PMS. In view of the failure of some PMS treatments in patients having PMDD, is it not obvious to one of ordinary skill in the art to administer a treatment taught to be effective for PMS, to a patient suffering from the different clinical indication of PMDD. It is important to note that "symptoms" are not treated; *diseases* are treated. Indeed, the Food and Drug Administration recognizes PMDD as a different clinical indication from PMS. A drug which is approved for

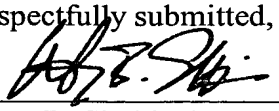
treatment of PMS is *not* approved for administration to patients having PMDD. This alone undercuts the entirety of the basis upon which the rejection is made.

Moreover, it is submitted that the Office Action misinterprets the teachings of the prior art, at the time the present application was filed. Attention is directed to the attached declaration under 37 C.F.R. §1.132, explaining that, contrary to the indication in the Office Action, the art actually teaches away from the administration of oral contraceptives, much less those containing gestagen and estrogen, to treat PMS, much less PMDD. As discussed at length in the declaration, the prior teaches that persons taking oral contraceptives were more likely, not less likely, to experience worsening of symptoms. Particular attention should be paid to the paragraph bridging pages 3 and 4 of the declaration criticizing the Dennertein paper. As explained in the declaration, the results of Dennertein, on an extremely small sample which may not even have been statistically significant, actually showed relatively *fewer* patients experienced improvement than those who did not. Moreover, a portion of the data of the reference referred to physical measures which were not relevant to a diagnosis of PMDD. In addition, the paper hypothesizes that the premenstrual symptoms are a result of an imbalance between estrogen and gestagen, and therefore does *not* in fact permit conclusions on the results of administering estrogen and progesterone *together*. Thus, as stated in the declaration, even if one of ordinary skill in the art would have recognized the idea of at least attempting to treat PMS with various oral contraceptive preparations, the evidence at the time suggested that such oral contraceptives did not work well and had no benefit treating the psychological symptoms associated with the diagnosis of PMDD. Moreover, as stated previously, even if it would have been obvious to employ a gestagen and estrogen in the treatment of PMDD (although it is not, as discussed at length above) one of ordinary skill in the art finds no motivation to select the particular gestagen, Drospirenone, claimed herein. Accordingly, it is submitted that more than ample basis to withdraw the rejection under 35 U.S.C §103 exists, and the same is respectfully requested.

The claims of the application are submitted to be in condition for allowance. However, if the Examiner has any questions or comments, she is cordially invited to telephone the undersigned at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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